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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/069,827
Filing Date: February 26, 2002
Appellant(s): DERAND ET AL.

MAILED
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GROUP 1700

Melissa W. Acosta
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 23 May 2007 appealing from the Office action mailed 06 June 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5935401	AMIGO	08-1999
5840388	KARGER ET AL.	11-1998
5958202	REGNIER ET AL.	09-1999
5250613	BERGSTROM ET AL.	10-1993
6183829	DAECHER ET AL.	02-2001
4690749	VAN ALSTINE ET AL.	09-1987

DE 197 53 847.9, ZIMMER ET AL., English Translation provided by Applicant, 06-1999

Malmsten, M. et al, "Effect of Chain Density on Inhibition of Protein Adsorption of Poly (ethylene glycol) Based Coatings", Journal of Colloid and Interface Science, 202, 507-517. (1998)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 2-5, 7, 8,10-13, 18-23, 28, 34, 35, 42, 43, and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amigo in view of Zimmer et al, Karger et al, and Regnier et al.

Regarding claim 7, Amigo discloses a microfluidic device (Column 6, line 46 - Column 8, line 21) comprising a set of one or more (Column 7, lines 29-34) covered microchannel structures (Column 7, lines 49-55) manufactured in the surface of a planar substrate (Column 3, line 36 - Column 4, line 9); wherein the microchannel structures comprise plural functional parts (e.g. branches; Column 7, lines 37-40) that are volume-defining units (Any channel defines the volume it occupies, by its nature); wherein non-specific adsorption and hydrophilicity are optimized by a coat exposing a non-ionic hydrophilic polymer on a part of the surface of at least one of the microchannel structures (Column 4, line 53 - Column 5, line 48); Also regarding the question of optimization, generally, differences in concentration (i.e. in this case, density, thickness, or other variable of the coating) or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Regarding claim 2, Amigo discloses the surface carrying the coat being made of organic material. (Column 3, line 36 - Column 4, line 22)

Regarding claim 3, Amigo discloses the surface of the planar substrate being made of plastic. (Column 4, lines 10-22)

Regarding claims 4 and 20, Amigo discloses the non-ionic hydrophilic polymer being attached to a polymer skeleton that is attached to the surface. (Column 4, lines 10-64)

Regarding claim 5, Amigo discloses the device comprising more than five covered microchannel structures. (Column 7, lines 29-31)

Regarding claim 8, Amigo discloses microchannel structures comprising a microcavity having a volume less than or equal to 1 μL. (Column 6, line 60 - Column 7, line 14; usual microchannel dimensions give a volume range of 0.02 - 2.5 μL)

Regarding claim 10, Amigo discloses the device being a round disk. (Column 7, lines 20-25)

Regarding claim 11, Amigo discloses the hydrophilic polymer comprising amide or ethylene oxy groups. (Column 5, lines 32-40)

Regarding claims 18 and 19, Amigo discloses the hydrophilic polymer comprising a plurality of amide groups, and being a polymerisate of monomers of acrylamide (i.e. polyacrylamide). (Column 5, lines 32-40)

Regarding claim 21, Amigo discloses covalent attachment between the hydrophilic polymer and the skeleton. (Column 4, lines 59-64)

Regarding claims 22 and 23, Amigo discloses the polymer skeleton being an organic polymer that is neutral. (Column 4, lines 32-40)

Regarding claim 28, Amigo discloses the surface of the planar substrate being made of a plastic that comprises a non-significant fluorescence for excitation

wavelengths in the interval of 200-800 nm and emission wavelengths in the interval of 400-900 nm. (Column 3, line 36 - Column 4, line 9)

Regarding claim 34, Amigo discloses the plastic substrate being based on a polymer of aliphatic monomers containing polymerizable carbon-carbon double bonds. (Column 3, lines 49-54)

Regarding claim 35, Amigo discloses the monomer being ethylene or propylene. (i.e. product is polyethylene or polypropylene; Column 3, lines 49-54)

Regarding claim 36, Amigo discloses mass transport of solutes and/or particles between different functional parts of the microchannel structure using electroendoosmosis (i.e. electroosmotic flow, EOF). (Column 4, line 65 - Column 5, line 16; Column 6, lines 21-45)

Regarding claims 42 and 43, Amigo discloses inorganic materials and polymers for the channel surfaces. (Column 3, lines 8-19 and 47-49; glass is disclosed)

Regarding claim 47, Amigo discloses solute transport. (Column 4, line 65 - Column 5, line 3; EOF of the solution will lead to solute transport)

Regarding claim 54, Amigo discloses a reaction taking place within the channels of his device. (e.g. Column 12, lines 30-34 of Column 6, lines 39-41) Any such channel with microscale dimensions can be called a "reaction microcavity".

Relevant to claim 7, Amigo does not explicitly disclose the device being in a dry state that is capable of being rehydrated, nor does he disclose surfaces of device parts having a sufficient hydrophilicity for liquid to enter the part once having passed the

entrance of the part. (i.e. by capillary forces) Amigo also does not explicitly disclose mass transport of solutes or particles between different functional parts of a microchannel structure using a liquid flow caused by non-electrokinetic forces. Relevant to claims 12 and 13, Amigo does not explicitly disclose a device comprising a polyhydroxy hydrophilic polymer (Claim 12), or a polyhydroxy polymer selected from among polysaccharides, polyvinyl alcohols, and poly(hydroxyl alkyl vinylether) polymers. (Claim 13)

Zimmer et al disclose the ability of capillaries with sufficiently hydrophilic surfaces, including polymer surfaces, to draw in aqueous materials upon contact. (Pages 5-8)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Amigo by specifically providing a hydrophilic surface (such as a hydrophilic polymer surface) at a channel opening to draw aqueous fluids in by capillarity, as taught by Zimmer et al, because it would facilitate sample introduction in some applications. (e.g. biosensor)

Karger et al disclose the use of a polyvinyl alcohol coating in electrophoresis capillaries in order to minimize adsorption of analytes to the capillary walls and control electroosmosis. (Column 1, line 50 - Column 2, line 39) (Claims 12 and 13) They also disclose the subsequent drying of the coated capillaries (Column 7, lines 1-39,

particularly lines 38-39), and the rehydrating of the capillaries for use in later analyses. (Column 7, line 40 - Column 8, line 43; rehydration would be inherent)

Addressing claim 7, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the invention of Amigo by providing the device in a dry state that is capable of being rehydrated, as taught by Karger et al, because it would facilitate device storage and shipping. The convenience of being able to store devices for later use, as compared to preparing the coatings immediately prior to use would have been obvious and highly desirable to one having ordinary skill in the art.

Addressing claims 12 and 13, it would have been obvious to one having ordinary skill in the art to modify the invention of Amigo by replacing his non-ionic hydrophilic coating with the polyvinyl alcohol coating taught by Karger et al, because Karger et al teach that it performs similar functions, and it would possess different reactivity that could facilitate a particular analysis. Selection of a known separation medium in capillary electrophoresis falls well within the level of ordinary skill in the art.

Regnier et al disclose bulk fluid motion caused by non-electrokinetic means. (Column 37, lines 53-59)

It would also have been obvious to one having ordinary skill in the art to further modify the device of Amigo by using a non-electrokinetic means of moving fluid within the channels, as taught by Regnier et al, because it would prevent electrophoretic bias in the injection procedure. Additionally, if the object of the application of the hydrophilic

coating was to minimize or substantially eliminate electroosmotic flow (See Amigo, Column 5, lines 9-16), then a non-electrokinetic means of bulk fluid motion would be required in order to have efficient fluid flow.

Also regarding claim 7 and the "adapted for mass transport of solutes and/or particles . . . caused by non-electrokinetic forces" limitation, this limitation is drawn primarily to an intended use of the device, as any fluid transport system is amenable to such means of transport. Amigo in fact discloses such non-electrokinetic fluid transport in preparing the device. (Column 9, lines 45-48) Such adaptation is considered to be present. The Regnier et al reference is primarily cited to show that such means of fluid movement in systems of this type was conventional in the art, even if this limitation were amended to more explicitly require it. In addition, Applicant's disclosure gives absolutely no indication that a non-electrokinetic means of fluid movement is a significant part of the claimed invention. The disclosure at Page 13, lines 4-22 describes suitable means of causing fluid flow, and lists electrokinetic means (e.g. electroendoosmosis and electrophoresis) and non-electrokinetic means, with no indication that either is preferable.

Also regarding claim 7 and the "self-suction" limitation, capillary action is a conventional technique for sample introduction in techniques using tubular capillaries, and its extension to microfluidic chips involves no inventive skill. Indeed, entry of liquid by "self-suction" would inherently result from bringing a drop of aqueous liquid in contact

with any inlet of a dry microfluidic system coated with a hydrophilic polymer, such as that resulting from the combination of Amigo and Karger et al.

Claims 14 and 24-26 rejected under 35 U.S.C. 103(a) as being unpatentable over Amigo, Zimmer et al, Karger et al, and Regnier et al as applied to claims 7 and 20 above, and further in view of Bergstrom et al. (US 5,250,613).

Amigo, Zimmer et al, Karger et al, and Regnier et al disclose a combined device as described in addressing claims 7 and 20 above.

None among Amigo, Zimmer et al, Karger et al, and Regnier et al explicitly disclose the use of a hydrophilic polymer that is a reaction product between ethylene oxide and a dihydroxy or a polyhydroxy compound (Claim 14), nor do they explicitly disclose the use of a polyamine skeleton (Claim 24), a polyethylene imine skeleton (Claim 25), or a skeleton with a molecular weight of 10,000 - 3,000,000 Da. (Claim 26)

Relevant to claim 14, Bergstrom et al disclose the use of a coating of an adduct of ethylene oxide and a dihydroxy or polyhydroxy compound as a hydrophilic polymer that prevents or reduces analyte adsorption to a surface. (Column 7, lines 20-24; Column 1, line 56 - Column 2, line 28)

Relevant to claims 24-26, Bergstrom et al disclose the use of a polyethylene imine skeleton with molecular weight of 10,000 - 1,000,000 Da. (Column 3, lines 15-49; Column 7, lines 41-52) Polyethylene imine is a polyamine.

Addressing claim 14, it would have been obvious to one having ordinary skill in the art to modify the invention of Amigo by replacing his non-ionic hydrophilic coating with a coating of an adduct of ethylene oxide with dihydroxy or polyhydroxy compounds, as taught by Bergstrom et al, because Bergstrom et al teach that it performs similar functions, and it would possess different reactivity that could facilitate a particular analysis. Selection of a known separation medium in capillary electrophoresis falls well within the level of ordinary skill in the art.

Addressing claims 24-26, it would have been obvious to one having ordinary skill in the art to further modify the invention of Amigo by replacing his non-ionic hydrophilic coating with a biopolymer (e.g. cellulose, starch) coating supported by a skeleton of polyethylene imine with a molecular weight of 10,000 - 1,000,000, as taught by Bergstrom et al, because Bergstrom et al teach that it performs similar functions, and it would possess different reactivity that could facilitate a particular analysis. Selection of a known separation medium in capillary electrophoresis falls well within the level of ordinary skill in the art.

Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amigo, Zimmer et al, Karger et al, and Regnier et al as applied to claim 11 above, and further in view of Malmsten et al.

Amigo, Zimmer et al, Karger et al, and Regnier et al disclose a combined device as described in addressing claim 11 above.

None among Amigo, Zimmer et al, Karger et al, and Regnier et al explicitly disclose the use of a polymer comprising one or more blocks of polyoxyethylene chains (Claim 15), the use of polyethylene glycol as the hydrophilic polymer (Claim 16), or the use of polyethylene glycol with a methoxy group at the end that does not bind to the surface as the hydrophilic polymer. (Claim 17)

Malmsten et al disclose the use of polyethylene glycol as a hydrophilic coating for minimizing protein adsorption in biological applications. (Abstract, Introduction) A variety of polyethylene glycol was disclosed that had methoxy end groups that do not bind the surface (Tables 2 and 3, Pages 512-515)

It would have been obvious to one having ordinary skill in the art to further modify the invention of Amigo by replacing his non-ionic hydrophilic coating with the polyethylene glycol coating taught by Malmsten et al, because Malmsten et al teach that it performs similar functions, and it would possess different reactivity that could facilitate a particular analysis. Selection of a known separation medium in capillary electrophoresis falls well within the level of ordinary skill in the art.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Amigo, Zimmer et al, Karger et al, and Regnier et al.

Amigo, Zimmer et al, Karger et al, and Regnier et al disclose a combined device as described in addressing claim 7 above. Amigo also suggests performing affinity assays in his system. (Column 10, lines 28-47)

Regnier et al also disclose a method of performing an analytical assay (Example 2) comprising preparing a sample (Column 42, lines 63-65); running an assay reaction (Column 42, line 65 - Column 43, line 7), and detecting the result of the assay reaction, wherein the result is a measure of the activity of the sample. (Column 43, lines 12-20) Regnier also states that "the method of the invention can be carried out in any conventional capillary electrophoresis system." (Column 42, lines 8-10)

It would have been obvious to one having ordinary skill in the art to use the device disclosed by Amigo, Zimmer et al, Karger et al, and Regnier et al in an assay procedure such as that disclosed by Regnier et al, because Regnier et al suggest performing it in any conventional system, including microfluidic devices (Column 42, lines 8-12), and Amigo suggests preparing a device with affinity agent in the coating (Column 10, lines 28-47), providing strong suggestion of its suitability for use in such assays. It appears to the examiner that any conventional assay procedure making use of the device of Amigo (with affinity agents) would read on the claim, as the sample preparation and running steps would be inherent in any procedure, and the detected result of any assay would provide a measure of sample activity.

Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Amigo, Zimmer et al, Karger et al, and Regnier et al as applied to claim 35 above, and further in view of Daecher et al.

Amigo, Zimmer et al, Karger et al, and Regnier et al disclose a combined device as described above in addressing claim 35. Amigo also discloses the suitability of a broad range of polymers for forming the substrate of his device, suggesting the use of other suitable materials ("and the like" - Column 3, lines 36-60)

None among Amigo, Zimmer et al, Karger et al, and Regnier et al explicitly disclose using a norbornene as a monomer.

Daecher et al disclose the preparation of polymer sheets suitable for forming microfluidic systems (Column 9, lines 55-65) using polymers made using norbornene monomers. (Column 14, lines 9-32)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Amigo by forming it using a polymer sheet made using norbornene monomers, as taught by Daecher et al, because Amigo suggested the use of other suitable polymers, and Daecher et al teach the suitability of these materials for forming microfluidic devices.

Claims 7 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karger et al in view of Zimmer et al, Van Alstine et al, and Regnier et al.

Relevant to claim 7, Karger et al disclose a microfluidic device (Column 2, lines 27-32) comprising covered microchannel structures (Column 9, line 18 - Column 10, line 4) manufactured in the surface of a planar substrate (Column 2, lines 27-32), wherein non-specific adsorption and hydrophilicity are altered by a coat exposing a non-ionic

hydrophilic polymer on a part of the surface of at least one of the microchannel structures. (Column 2, lines 20-39) They also disclose the subsequent drying of the coated capillaries (Column 7, lines 1-39, particularly lines 38-39), and the rehydrating of the capillaries for use in later analyses. (Column 7, line 40 - Column 8, line 43; rehydration would be inherent)

Relevant to claim 27, Karger et al disclose the substrate being made of plastic (Column 6, lines 15-22), and preparation of a bare capillary surface (silica) with acid to ensure proper surface functionalization for the coating reaction. (Column 7, lines 1-11)

Karger et al do not explicitly disclose plural functional parts, at least one of which is coated with hydrophilic polymer into which aqueous liquid can enter by self-suction when the liquid has passed the entrance of the functional part, or mass transport of solutes or particles between different functional parts of a microchannel structure using a liquid flow caused by non-electrokinetic forces. (Claim 7), nor do they disclose a plastic part surface without coat being hydrophilized by a plasma treatment or oxidation agent in order to introduce functional groups that allow for a subsequent attachment of a coat onto the part surface. (Claim 27)

Relevant to claim 7, Regnier et al disclose microfluidic systems of conventional design (i.e. injection tee, Figures 8-10), with plural functional parts (i.e. branches) that define their volume. Regnier et al also disclose bulk fluid motion caused by non-electrokinetic means. (Column 37, lines 53-59)

Relevant to claim 7, Zimmer et al disclose the ability of capillaries with sufficiently hydrophilic surfaces, including polymer surfaces, to draw in aqueous materials upon contact. (Pages 5-8)

Relevant to claim 27, Van Alstine discloses the preparation of a plastic substrate for coating by plasma treatment, in order to introduce reactive surface groups. (Column 6, lines 14-21 and 31-39)

Regarding claim 7, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Karger by specifically using the conventional injection tee used for electrophoresis in microfluidic devices, as taught by Regnier et al, because it provides simple control of the injected sample volume, as taught by Regnier at Column 35, lines 28-33. Such injection tees were the basic conventional geometry used in the field of microfluidic systems at the time of the invention, and use of this geometry in the suggested microfluidic system of Karger et al (Column 2, lines 27-32) would have been obvious to a skilled artisan.

It would also have been obvious to one having ordinary skill in the art to further modify the device of Karger et al by using a non-electrokinetic means of moving fluid within the channels, as also taught by Regnier et al, because it would prevent electrophoretic bias in the injection procedure.

Regarding claim 7, it would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the device of Karger et al by providing a surface of sufficient hydrophilicity at a channel opening to draw aqueous

fluids in by capillarity, as taught by Zimmer et al, because it would facilitate sample introduction in some applications. (e.g. biosensor) Capillary action is a conventional technique for sample introduction in techniques using tubular capillaries, and its extension to microfluidic chips involves no inventive skill. Indeed, entry of liquid by "self-suction" would inherently result from bringing a drop of aqueous liquid in contact with any inlet of a dry microfluidic system coated with a hydrophilic polymer, such as that disclosed by Karger.

Regarding claim 27, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Karger et al by preparing the plastic substrate for coating by plasma treatment, as taught by Van Alstine et al, because it would provide a dry, less labor-intensive means of surface preparation.

Also regarding the question of optimization, generally, differences in concentration (i.e. in this case, density, thickness, or other variable of the coating) or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

(10) Response to Argument

(A) Rejection of claims 2-5, 7, 8, 10-13, 18-23, 28, 34, 35, 42, 43, and 54 under 35 U.S.C. §103(a) as unpatentable over Amigo (US 5,935,401) in view of Zimmer et al (DE 197 53 847.9), Karger et al (US 5,840,388), and Regnier et al. (US 5,958,202)

Section 1b: Level of ordinary skill in the art

Appellant argues that the rejections under 35 U.S.C. §103(a) are "fatally flawed as a mater [sic] of law", because the level of ordinary skill in the art was not explicitly addressed in the rejections. At the outset, the Examiner points out that there is not and never has been an absolute requirement for such an explicit statement resolving the level of ordinary skill in the art. Furthermore, each rejection made under 35 U.S.C. 103(a) provides a statement to the effect that the Examiner has considered each grounds from the perspective of those having ordinary skill in the art at the time the invention was made. From this perspective, the Examiner's position is that each combination would have been obvious to such a person having ordinary skill in the art.

At no earlier point in prosecution has Appellant raised the issue of resolving the level of ordinary skill in the art. Nor has Appellant presented any arguments that the level used by the Examiner in formulating the rejections is not appropriate. Appellant simply argues that the level of ordinary skill was not explicitly resolved.

Note MPEP §2141.03, which states in part that if the only facts of record pertaining to the level of skill in the art are found within the prior art of record, the court has held that an invention may be held to have been obvious without a specific finding

of a particular level of skill where the prior art itself reflects an appropriate level. *Chore-Time Equipment, Inc. v. Cumberland Corp.*, 713 F.2d 774, 218 USPQ 673 (Fed. Cir. 1983). See also *Okajima v. Bourdeau*, 261 F.3d 1350, 1355, 59 USPQ2d 1795, 1797 (Fed. Cir. 2001) and *Union Carbide Corp. v. American Can Co.*, 724 F.2d 1567, 220 U.S.P.Q. 584 (Fed. Cir. 1984). It is the Examiner's position that the references cited in the rejections reflect such an appropriate level of skill, as the principles of their teachings would certainly be understood by those working in the fields to which they pertain. Such skilled artisans would therefore have been able to apply such teachings, as presented in the rejections under appeal.

<u>Section 1c(i): Amigo</u>

Regarding the teachings of Amigo, Appellant further argues that one of ordinary skill in the art would have recognized that a "volume defining unit" as claimed is "structured to permit a specific amount of fluid to progress through the unit to subsequent microstructures (i.e. fluid metering)". ("Volume Defining Unit" section of Page 10) Nowhere in the instant specification is such a definition provided, nor is there any discussion of a "volume defining unit", other than to list it among numerous "functional parts" that can be included in the device. (See Specification Page 12, line 24 – Page 13, line 2) Therefore, the only reasonable reading of the limitation is to consider a "volume defining unit" to be a structure that defines a volume. Any channel will inherently define a volume, specifically the volume corresponding to the channel's walls. The limitation is considered to be clearly present in the device of Amigo. In this section Appellant also asserts that a functional limitation "is disregarded as a convenient but

impermissible way to avoid one of the many insufficiencies of the pending obviousness rejection." Aside from the other inaccuracies of this statement, it is not clear how any such limitation has been disregarded, as Examiner's position is that a volume defining unit is taught by the prior art.

Regarding the Non-Electrokinetic Fluid Transport limitation, Appellant argues that there is no teaching in Amigo that microchannel structures are to be coated by polymers after a cover is attached. The relevance of this statement is ambiguous, but the Examiner would like to emphasize that Amigo teaches that the channels can be open or closed (e.g. Column 6, lines 46-53; Column 7, lines 49-55) and the contacting step that is terminated by the non-electrokinetic flow cited at Column 9, lines 45-48 is disclosed as involving flow of reagents through the device. (Column 9, lines 29-33) It seems clear that Amigo's teaching of ending such a contacting step by "flushing nitrogen or air under pressure" directly suggests blowing pressurized air or nitrogen through the device. With the closed channel embodiment, this clearly corresponds to non-electrokinetic flow as claimed. The Examiner would also like to reiterate that the "adapted for mass transport of solutes and/or particles . . . caused by non-electrokinetic forces" limitation, is drawn primarily to an intended use of the device, as any fluid transport system is amenable to such means of transport. Since Amigo discloses such non-electrokinetic fluid transport in preparing the device (Column 9, lines 45-48), such adaptation is considered to be present. Appellant further emphasizes that such non-electrokinetic flow is recited as being "between" functional parts. The term "functional part" in the absence of further description is broad enough to apply simply to channel sections, openings,

intersections, etc. Intersected channels having termini are taught by Amigo (Column 7, lines 35-48) Flow clearly can take place between such intersections and termini via the channels, and such flow therefore would take place between "functional parts", broadly defined. The claimed adaptation is therefore clearly present.

Section 1c(ii): Zimmer et al.

Regarding Zimmer et al, Appellant asserts that the channels of Zimmer et al are not capillaries, because they have widths of several millimeters. Appellant fails to mention that the heights of these channels are preferably on the order of tens of micrometers (Page 5, lines 4-12), which clearly corresponds to capillary dimensions. Zimmer et al has been cited to show the conventionality of "self-suction" in devices having channels of microscale dimension. Contrary to Appellant's unsupportable assertion, the teaching is clearly present, as cited in the rejection.

Section 1c(iii): Karger et al.

Regarding the limitation to a device "being in a dry state that is capable of being rehydrated", Appellant argues that "there is no extrinsic evidence cited or reasoning advanced to support the position that Karger et al. inherently meets this limitation." At the outset, the Examiner notes that anything that is "dried" from a wet state is capable of being rehydrated upon contact with water. Rehydration is not a positive limitation in instant claim 7. As a courtesy, to demonstrate that such devices are known, the Examiner chose to address the limitation beyond statement of this fact. The Examiner's stated position is that rehydration of the dried capillary would be inherent in the carrying out of the procedures described at column 7, line 40 – Column 8, line 43 of Karger et al.

(Note Page 7, 3rd full paragraph of the Final Office Action of 6 June 2006) Example I of Karger et al (Column 7, lines 1-39), teaches drying of capillaries having hydrophilic polymeric coatings, as cited in the rejection. Examples II-X of Karger et al use the capillaries of Example I in electrophoretic procedures involving buffers that would be understood by one having ordinary skill in the art to be aqueous. Providing an aqueous buffer to a previously dried capillary would clearly inherently rehydrate the device. Anyone having any skill in the art would have recognized this in reading the Karger et al reference. Appellant's position is therefore clearly in error.

<u>Section 1c(iv): Regnier et al</u>

Appellant argues that Regnier et al do not meet the limitation to the device being "adapted for mass transport of solutes and/or particles between different functional parts of each microchannel structure by a liquid flow caused by non-electrokinetic forces." As noted above, Amigo is considered to meet this limitation due to the teaching of non-electrokinetic flow within the channels in fabrication of the device. However, in addition to this, the Regnier et al reference was cited primarily to show that such means of fluid movement in systems of this type was conventional in the art, even if this limitation were amended to more explicitly require it. As described above, the term "functional part" in the absence of further description is broad enough to apply simply to channel sections, openings, intersections, etc. Intersected channels having termini are taught by Amigo (Column 7, lines 35-48) Flow clearly can take place between such intersections and termini via the channels, and such flow therefore would take place between "functional parts", broadly defined. The claimed adaptation is therefore clearly present.

In addition, the Examiner notes that Applicant's disclosure gives absolutely no indication that a non-electrokinetic means of fluid movement is a significant part of the claimed invention. The disclosure at Page 13, lines 4-22 describes suitable means of causing fluid flow, and lists electrokinetic means (e.g. electroendoosmosis and electrophoresis) and non-electrokinetic means, with no indication that either is preferable.

Section 1c(v): Amigo plus Karger et al

Appellant cites the Office Action of 6 June 2006 as addressing the self suction limitation at page 7, last paragraph. This is in error, since this paragraph describes the coatings, drying, and rehydration taught by Karger et al. The self suction limitation is irrelevant to this portion of the rejection. The quotation made by Appellant is not present at this point in the rejection, "entry of liquid by 'self-suction' would inherently result" is excerpted from page 9, which states essentially that contact of liquid to a dry microfluidic channel having a hydrophilic coating would inherently result in the instant "self-suction". This is not a method claim. A step of entry of fluid by self-suction is not required by the claim. The device described by the combination has the claimed capability, as would have been recognized by anyone having ordinary skill in the art.

Section 1d: Non-Specific Adsorption and Hydrophilicity

In re Aller was cited by the Examiner as pertinent to the claim limitation reciting that parameters "have been optimized". Amigo clearly is concerned with reduction of non-specific adsorption within the hydrophilic coatings he teaches. (Column 5, lines 29-48) The only language of the claim regarding how "nonspecific adsorption and

hydrophilicity have been optimized" is the recitation of provision of a hydrophilic coating that is in no way distinct from that of Amigo. The limitation amounts essentially to an assertion of superior performance, having no basis whatsoever in the structure recited in the claim. This limitation therefore provides no patentable distinction from the prior art.

Section 1e: Teaching, Suggestion, or Motivation to Combine or Modify the Art

At the outset, the Examiner notes that the courts have foreclosed the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 USPQ2d at 1396)(available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf)

Section 1e(i): Amigo in view of Zimmer et al

Appellant argues that there is insufficient motivation for the combination. The Examiner maintains the position that the device of Amigo has the claimed capability, as described above, simply by virtue of being a capillary device. Furthermore, if weight has to be given to the mere intended use relied upon by Appellant, Zimmer et al demonstrates the conventionality and desirability of using capillary forces (i.e. self-suction) for sample introduction into analytical devices. The remainder of Appellant's arguments in this section fails to conjure a patentable limitation.

Section 1e(ii): Amigo in view of Karger et al

Again, Appellant argues insufficient motivation, arguing that the rejection is conclusory and unsubstantiated. Karger et al demonstrate the drying of the coatings

within capillaries for later use in Examples I-X. There can be little doubt that storage and shipment of devices containing liquids presents significant problems relative to storage and shipment of dry devices, particularly in the case of microfluidic devices, which universally comprise openings for sample introduction, electrodes, and the like. Anyone of skill in the art would have recognized that storage or shipment of a wet device would require considering solvent evaporation and secure positioning of the device for prevention of spillage and that these concerns do not apply to a dry device. Therefore, the motivation for drying a microfludic device having a hydrophilic polymer coating, as taught by Karger et al, is present.

Section 1e(iii): Amigo in view of Regnier et al

In this instance, Appellant again argues that the rejection is conclusory and unsubstantiated, this time relative to the term "electrophoretic bias". As with the "self-suction" limitation, it is the Examiner's position that the claimed configuration is present in Amigo, since even a simple tube is configured to allow non-electrokinetic flow, but if weight is to be given to the functional language, Regnier et al demonstrate the conventionality of non-electrokinetic flow in microfluidic systems. As Appellant is certainly aware, as was anyone of ordinary skill in the art at the time this application was filed, electrophoretic bias is an effect peculiar to electrokinetic sample injection, in which sample components of differing electrophoretic mobility migrate into a capillary (or injection tee, in conventional microfluidic systems) at differing rates, leading to injection of a nonrepresentative sample. Non-electrokinetic flow means (e.g. pressure, vacuum

driven flow) do not suffer from this drawback. This provides clear motivation for use of non-electrokinetic flow means.

Regarding the arguments of the "Non-electrokinetic Flow" section of page 19, in which Appellant takes issue with the presupposition that bulk flow is required in the device of Amigo et al, the Examiner must point out that fluids need to be introduced into the device. Although electrophoresis as an analytical process does not require bulk flow, the introduction of fluids necessary for electrophoresis (i.e. buffers, samples) require bulk flow. Non-electrokinetic means would be necessary for providing this flow in a device, such as Amigo's, in which EOF is substantially eliminated. (Amigo, Column 5, lines 9-13)

<u>Section 2: Claim 42</u>

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

Appellant appears to be arguing that only a polymeric base material is taught by Amigo. This is incorrect, as Amigo clearly discloses glass materials and inorganic polymers at Column 3, lines 8-19 and 47-49, as cited in the action. Karger et al also discloses coated glass channels. (Example I)

<u>Section 3: Claim 43</u>

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

Appellant argues that there is no teaching of an inorganic polymer in Amigo. Amigo suggests at Column 3, lines 47-49 that the polymer may not be organic. There is

no teaching in the instant specification as to what would be considered an inorganic polymer. Note also that glass typically comprises an amorphous network of Si-O and metal-O bonds, which reads on an inorganic polymer.

(B) Rejection of claims 14 and 24-26 under 35 U.S.C. §103(a) as unpatentable over Amigo in view of Zimmer et al, Karger et al, and Regnier et al, further in view of Bergstrom et al. (US 5,250,613)

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

Appellant argues that the disclosed applications of the coating taught by Bergstrom are somehow incompatible with Amigo, because Bergstrom does not teach electrophoresis. Note however, that Amigo teaches that his devices can be used in precisely the type of affinity analyses taught by the portion of Bergstrom et al cited by Appellant. (Amigo, column 10, lines 28-47) The coatings of Bergstrom et al similarly address the problem of nonspecific adsorption addressed by Amigo et al. The combination is clearly proper.

(C) Rejection of claims 15-17 under 35 U.S.C. §103(a) as unpatentable over Amigo in view of Zimmer et al, Karger et al, and Regnier et al, further in view of Malmsten et al. (J. Colloid Interface Sci. reference)

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

Appellant further argues that Malmsten et al teach nothing related to electrophoresis, and this renders the combination invalid. The Examiner maintains that Malmsten et al teach that the PEG coatings perform the same function as the coatings of Amigo, and that selection among known equivalents has been held to be obvious.

(D) Rejection of claim 30 under 35 U.S.C. §103(a) as unpatentable over Amigo in view of Zimmer et al, Karger et al, and Regnier et al.

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

Appellant relies on the arguments concerning claim 7, which were also addressed above in their entirety.

(E) Rejection of claim 45 under 35 U.S.C. §103(a) as unpatentable over Amigo in view of Zimmer et al, Karger et al, and Regnier et al, further in view of Daecher et al. (US 6,183,829)

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

Appellant relies on the arguments concerning claim 7, which were also addressed above in their entirety.

Appellant further argues that Daecher et al does not specifically teach adaptation of norbornene-based plastics for microfluidic devices, and that the reference is concerned with manufacturing CDs, as opposed to the microfluidic devices of the

instant invention. The microfluidic applications of the sheets taught by Daecher et al are quite clearly taught at Column 9, lines 55-65, and these applications correspond to precisely the type of applications disclosed by Amigo. The generic "polyolefin" material listed as suitable takes in norbornenes. Daecher et al then discloses norbornene monomers among the materials suitable for the process he teaches for making the sheet of the invention. (Column 14, lines 9-32) Note also that the "long list" of compounds given by Daecher et al seems comparable to the large number of compounds included in Appellant's own specification (Page 15, line 9 – Page 16, line 29)

(F) Rejection of claims 7 and 27 under 35 U.S.C. §103(a) as unpatentable over Karger et al in view of Zimmer et al, Van Alstine et al (US 4,690,749), and Regnier et al.

<u>Section 1a:</u>

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

<u>Section 1b(i): Karger et al</u>

Regarding covered microstructures, Appellant focuses on Karger et al's discussion of "open grooves", but conveniently ignores the language of claim 1 requiring a "microcapillary column" having "an interior cavity". The grooves of a conventional microfluidic system are opened on one plate, with a cover conventionally attached to protect the contents from contamination, etc. Note Amigo and Regnier et al as examples demonstrating the conventionality of this. Anyone of ordinary skill reading

Karger would have recognized covered microchannels within the scope of the disclosure, given the context of claim 1 and Column 2, lines 28-30.

Regarding Drying and Rehydrating, Appellant again takes the unsupportable position that Examples II-X of Karger et al, which add buffer solutions to previously dried capillaries made in Example I, somehow do not inherently rehydrate these capillaries. Example I of Karger et al (Column 7, lines 1-39), teaches drying of capillaries having hydrophilic polymeric coatings, as cited in the rejection. Examples II-X of Karger et al use the capillaries of Example I in electrophoretic procedures involving buffers that would be understood by one having ordinary skill in the art to be aqueous. Providing an aqueous buffer to a previously dried capillary would clearly inherently rehydrate the device. Anyone having any skill in the art would have recognized this in reading the Karger et al reference. Appellant's position is therefore clearly in error.

<u>Section 1b(ii): Regnier et al</u>

Regarding the teachings of Regnier et al, Appellant argues that one of ordinary skill in the art would have recognized that a "volume defining unit" as claimed is "structured to permit a specific amount of fluid to progress through the unit to subsequent microstructures (i.e. fluid metering)". ("Volume Defining Unit" section of Page 10) Nowhere in the instant specification is such a definition provided, nor is there any discussion of a "volume defining unit", other than to list it among numerous "functional parts" that can be included in the device. (See Specification Page 12, line 24 – Page 13, line 2) Therefore, the only reasonable reading of the limitation is to consider a "volume defining unit" to be a structure that defines a volume. Any channel will

inherently define a volume, specifically the volume corresponding to the channel's walls. The limitation is considered to be clearly present in the device of Regnier. In this section Appellant also asserts that a functional limitation "is disregarded as a convenient but impermissible way to avoid one of the many insufficiencies of the pending obviousness rejection." Aside from the other inaccuracies of this statement, it is not clear how any such limitation has been disregarded, as Examiner's position is that a volume defining unit is taught by the prior art.

Section 1b(iii): Zimmer et al

Regarding Zimmer et al, Appellant asserts that the channels of Zimmer et al are not capillaries, because they have widths of several millimeters. Appellant fails to mention that the heights of these channels are preferably on the order of tens of micrometers (Page 5, lines 4-12), which clearly corresponds to capillary dimensions. Zimmer et al has been cited to show the conventionality of "self-suction" in devices having channels of microscale dimension. Contrary to Appellant's unsupportable assertion, the teaching is clearly present, as cited in the rejection.

Section 1c: Teaching, Suggestion, or Motivation to Combine or Modify the Art

At the outset, the Examiner notes that the courts have foreclosed the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 USPQ2d at 1396)(available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf)

Section 1c(i) Karger et al in view of Regnier et al

Appellant argues that the rejection is conclusory and unsubstantiated, relative to the term "electrophoretic bias". Along with the teaching of non-electrokinetic flow in microfluidic devices, Regnier is cited as teaching typical microfluidic device geometry (e.g. Figures 8-10), which contain multiple functional parts (i.e. channels, intersections, reservoirs) Karger et al is silent concerning the configuration of the disclosed channel system, and the Examiner's position that is apparently uncontested by Appellant, is that configuration of the microfluidic device of Karger et al according to the teachings of Regnier et al would have been obvious. It is the Examiner's position that the claimed adaptation "for mass transport of solutes and/or particles between different functional parts of each microchannel structure by a liquid flow caused by non-electrokinetic forces" is present in this structure, since even a simple tube is configured to allow non-electrokinetic flow, but if weight is to be given to the functional language, Regnier et al demonstrate the conventionality of non-electrokinetic flow in microfluidic systems.

Particular to the "electrophoretic bias" arguments, as Appellant is certainly aware, as was anyone of ordinary skill in the art at the time this application was filed, electrophoretic bias is an effect peculiar to electrokinetic sample injection, in which sample components of differing electrophoretic mobility migrate into a capillary (or injection tee, in conventional microfluidic systems) at differing rates, leading to injection of a nonrepresentative sample. Non-electrokinetic flow means (e.g. pressure, vacuum driven flow) do not suffer from this drawback. This provides clear motivation for use of non-electrokinetic flow means.

<u>Section 1c(ii) Karger et al in view of Zimmer et al</u>

Appellant argues that there is insufficient motivation for the combination. The Examiner maintains the position that the device of Karger et al has the claimed capability, simply by virtue of being a capillary device. Furthermore, if weight has to be given to the mere intended use relied upon by Appellant, Zimmer et al demonstrates the conventionality and desirability of using capillary forces (i.e. self-suction) for sample introduction into analytical devices. The remainder of Appellant's arguments in this section fail to conjure a patentable limitation.

Section 1c(iii) Optimization of Karger et al

In re Aller was cited by the Examiner as pertinent to the claim limitation reciting that parameters "have been optimized". Karger et al clearly is concerned with reduction of non-specific adsorption within the hydrophilic coatings he teaches. (e.g. Column 2, lines 37-39)) The only language of the claim regarding how "nonspecific adsorption and hydrophilicity have been optimized" is the recitation of provision of a hydrophilic coating that is in no way distinct from that of Karger et al. The limitation amounts essentially to an assertion of superior performance, having no basis whatsoever in the structure recited in the claim. This limitation therefore provides no patentable distinction from the prior art.

Section 2a

Appellant's arguments concerning the level of ordinary skill in the art were addressed above.

Sections 2b-2c(iii)

Appellant relies on arguments concerning claim 7, which were addressed in the other portions of Section F of the Examiner's answer, above.

Section 2c(iv) Karger et al in view of Van Alstine et al

Appellant again argues that the grounds for rejection are conclusory and unsubstantiated. The Examiner cites Van Alstine et al as teaching an alternative means for preparing a substrate to have functional groups allowing subsequent functionalization. Karger et al perform an acid treatment to silica capillaries (Column 7, lines 1-11) to provide such reactive groups, but do not teach a specific method for preparing the polymeric surfaces that are also disclosed. (Column 6, lines 15-22) Van Alstine teaches using a plasma treatment as claimed for providing the necessary functionalization. (Column 6, lines 14-21 and 31-39) A plasma process would have been recognized a simpler than acid treatment in some respects, as no washing or drying of the surface is required after functionalization. The motivation is considered valid. The Examiner also points out that this procedure is functionally equivalent to the acid wash procedure of Karger et al, in that both are specifically adapted for producing reactive surface functionalities that bind polymeric coatings to these surfaces in capillary systems. Such selection among art-recognized equivalents has also been determined to be obvious to those of ordinary skill in the art. Note MPEP §2144.06.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Jeffrey T. Barton

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